

SUPPLEMENTARY MATERIAL

Table S1. Baked milk oral food challenge.

Steps	Amount Baked milk cookie	CMP (g)	CM volumen (ml)	Interval (minutes)
1	$\frac{1}{8}$	0.0375	1.1 ml	30
2	$\frac{1}{4}$	0.075	2.25 ml	30
3	$\frac{1}{2}$	0.15	4.5 ml	30
4	1	0.275	9 ml	30
5	2	0.55	18 ml	180 observation

Shows the oral food challenge protocol used.

Table S2. Clinical criteria for the diagnosis of anaphylaxis based on Muraro *et al.* (27).

Criterion	Description	Sub-criteria
1	Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue or both (e.g. generalized hives, pruritus or flushing, swollen lips-tongue-uvula)	And at least one of the following: a. Respiratory compromise (e.g. dyspnoea, bronchospasm, stridor, hypoxia) b. Cardiovascular compromise (e.g. hypotension, collapse)
2	Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours)	a. Involvement of the skin or mucosal tissue (e.g. generalized hives, itch, flushing, swelling) b. Respiratory compromise (e.g. dyspnoea, bronchospasm, stridor, hypoxia) c. Cardiovascular compromise (e.g. hypotension, collapse) d. Persistent gastrointestinal symptoms (e.g. crampy abdominal pain, vomiting)
3	Hypotension after exposure to known allergen for that patient (minutes to several hours)	Hypotension for children is defined as systolic blood pressure <70 mmHg from 1 month to 1 year, [$<70 \text{ mmHg} + (2 \times \text{age})$] from 1 to 10 years, <90 mmHg from 11 to 17 years

Shows the criteria used for the diagnosis of anaphylaxis based on Muraro A, *et al* 2007.

Note: Anaphylaxis is highly likely when any one of the above three criteria are fulfilled.

Adapted from Muraro *et al* (27).

Table S3 Grading of the severity of anaphylactic reactions based on Muraro *et al.*

Grade	Skin	GI tract	Respiratory	Cardiovascular	Neurological
1 Mild	Sudden itching of eyes and nose, generalized pruritus, flushing, urticaria, angioedema	Oral pruritus, oral "tingling", mild lip swelling, nausea or emesis, mild abdominal pain	Nasal congestion and/or sneezing, rhinorrhea, throat pruritus, throat tightness, mild wheezing	Tachycardia (increase > 15 beats/min)	Change in activity level plus anxiety
2 Moderate	Any of the above	Any of the above, crampy abdominal pain, diarrhea, recurrent vomiting	Any of above, hoarseness, "barky" cough, difficulty swallowing, stridor, dyspnea, moderate wheezing	As above	"Light headedness" feeling of "pending doom"
3 Severe	Any of the above	Any of the above loss of bowel control	Any of the above, cyanosis or SpO2 \leq 92%, respiratory arrest	Hypotension* and/or collapse, dysrhythmia, severe bradycardia and/or cardiac arrest	Confusion, loss of consciousness

Shows the grading of severity suggested for anaphylaxis according to Muraro A et al. The severity score should be based on the organ system most affected.

Hypotension defined as systolic blood pressure: 1 month to 1 year <70 mmHg; 1-10 years: (70 mmHg + [2 x age]); 11-17 years <90 mmHg. Modified from Muraro (27)

Table S4. Doses of reactivity in the OFC-CM.

Dosis	Mean	SD	Min	ED01	ED05	ED10	ED25	ED50	ED75	Max
ml	26,08	35,24	0,3	0,3	0,3	1,0	3,0	9,0	30	100
g protein	0,78	1,06	0,009	0,01	0,01	0,03	0,09	0,27	0,9	3

Shows the reactivity threshold in the OFC-CM in BM-Tolerant.

The effective dose (ED) calculations presented in this study are based on a limited sample size of 32 BM-tolerant patients. The estimates for ED50, ED25, and ED75 can be confidently used to describe the general tendency of the data and are typically reliable indicators of the range within which most reactions occur.

Other estimates (ED01, ED05...) offer an initial approximation of reactivity thresholds, they should be interpreted with caution due to the low statistical reliability inherent in a small sample size. This implies that the results may not be significant or statistically robust. Additional studies with larger cohorts are necessary to validate these findings and provide more precise estimates.

Table S5. Comparative characteristics between patients <3 years and >3 years.

	Under 3 years old (n=25)	Over 3 years old(n=25)	p-value
SPT casein (mm) (mean [Me; IQR])	5.5 [5.6; 4.88]	6 [5.7; 4.06]	0.629
SPT milk (mm) (mean [Me; IQR])	8.6 [8.4; 3.93]	9 [9.3; 4.25]	0.601
SPT alfa (mm) (mean [Me; IQR])	9.1 [7.6; 5.72]	8.8 [7.9; 7.85]	0.810
SPT beta (mm) (mean [Me; IQR])	6.2 [5.8; 4.37]	7.1 [6.8; 4.46]	0.406
Casein sIgE (kU/L) (mean [Me; IQR])	3.8 [1.4; 4.63]	32.8 [6; 22.24]	0.007
Milk sIgE (kU _A /L) (mean [Me; IQR])	12.6 [3.2; 13.78]	35.7 [9.1; 24.71]	0.461
Alfa sIgE (kU _A /L) (mean [Me; IQR])	5.7 [0.4; 2.48]	10.4 [1.5; 8.86]	0.370
Beta sIgE (kU _A /L) (mean [Me; IQR])	6.7 [0.6; 3.52]	8.2 [0.8; 6.27]	0.789
	Under 3 years old (n=16)	Over 3 years old (n=10)	p-value
Casein IgG ₄ (mg _A /L) (mean [Me; IQR])	0.5 [0.2; 0.34]	1.1 [0.4; 0.86]	0.285
Milk IgG ₄ (mg _A /L) (mean [Me; IQR])	9.9 [9.2; 1]	11.6 [10.4; 1.42]	0.188